Application No. 10/659,063
Filed: September 10, 2003
TC Art Unit: 1623
Confirmation No.: 3827

REMARKS

The Applicants' are appreciative of the effort of the Examiners to create the time for the above-indicated telephonic Examiners' Interview and for the consideration shown during the interview to the Applicants' arguments.

The Applicants agree with the Examiners' statement in the Interview Summary dated May 22, 2007, that Dr. Fink urged that the invention is directed to controlling and reducing inflammatory conditions, not for increasing inflammation, and that inflammation and infection are not synonymous terms and should be considered in context.

This paper is submitted to summarize the Applicants' arguments concerning the Lund et al. reference in a tabular format, side by side with the paragraphs of the publication that Examiner Henry cited in the Office Action mailed June 12, 2006, in support of his arguments. The Applicants hope that this presentation format (attached) will be useful.

In summary, Applicants argue that the Examiner has not made even a *prima facie* obviousness argument in rejecting Applicants' claims. Instead, Applicants submit that Lund et al. is a clear teaching away situation and that one of ordinary skill would never have been led to the Applicants' invention through any of the Lund et al. teachings.

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Applicants submit that all claims are in condition for allowance and such action is respectfully requested.

The Examiners are encouraged to telephone the undersigned attorney to discuss any matter that would expedite allowance of the present application.

Respectfully submitted,

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APPLICANTS' RECITATION OF ARGUMENT PRESENTED IN EXAMINER INTERVIEW 5/22/07

BROAD CLAIM

1. A method for treating an inflammatory condition, said method comprising the steps of:
providing a patient having an inflammatory condition; and
administering to said patient a therapeutically effective amount of a composition comprising cyclic adenosine diphosphate ribose (cADPR), or a functional analogue or derivative [agonist] thereof, in a form that is accessible to a receptor molecule, conveyed in a pharmaceutically acceptable carrier vehicle, wherein said composition *reduces* the degree of said *inflammatory condition* in said patient.

APPLICANTS' SUMMARY

Examiner's Arguments (from OA mailed 6/12/06, p. 3) and Applicants' Response	**Referenced Paragraphs from Lund et al., Pub. No. US 2002/0127646**
EXAMINER: Lund et al. disclose that modulators, such as agonists and antagonists, of CD38 enzyme activity and/or modulators of cADPR dependent calcium responses and chemotaxis can be used in the treatment of disorders including inflammation in a subject (see page 4, 2nd col. Paragraph [0032]). **APPLICANTS:** Paragraph [0032] mentions modulators such as "agonists and antagonists" in the same phrase. It does not acknowledge that an agonist and an antagonist of CD38 enzyme activity would have opposite effects. The last sentence of this paragraph recites a list of treatable disorders but gives no hint as to WHICH of the two (agonist or antagonist) would be effective against which disorder.	[0032] The present invention encompasses screening assays designed for the identification of modulators, such as agonists and antagonists, of CD38 enzyme activity and/or modulators of cADPR dependent calcium responses and chemotaxis. The invention further relates to the use of such modulators in the treatment of disorders based on the CD38 controlled migratory activity of cells to chemoattractants and inflammatory products. Such disorders include, but are not limited to, inflammation, ischemia, autoimmune disease, asthma, diabetes, arthritis, allergies, infections and organ transplant rejection.

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APPLICANTS: Paragraph [0032] is not specific as to which modulator is suggested for which condition. However, it can be interpreted in conjunction with [0013], which IS specific as to which modulator is suggested for which condition. [0013], first half of the paragraph, states that CD38 *antagonists* may be used in the *treatment* of *inflammation* among other disorders. [0013], in the second half of the paragraph, states that *agonists* of CD38 should be used when the subjects are "infected with pathogenic microorganisms," i.e., a condition in which *inflammatory agents are recruited and inflammation is induced to fight the infection.*	[0013, *first half*] Identified compounds may be used in the treatment of disorders where the migratory activity of CD38-expressing cells, such as hematopoietically-derived cells, contributes to the development of such disorders. Such disorders include, but are not limited to inflammation, ischemia, asthma, autoimmune disease, diabetes, arthritis, allergies or transplant rejection where inhibition of migratory activity using, for example, CD38 antagonists would be desired. [0013, *second half*] In contrast, in subjects infected with pathogenic microorganisms or immunosuppressed subjects it may be desirable to induce the migratory activity of hematopoietically-derived cells using, for example, agonists of CD38. Additionally, identified compounds may be used to treat pathogenic disorders resulting from infection with pathogenic micro-organisms expressing SM38 or structurally related homologous proteins.
EXAMINER: Furthermore, Lund et al. disclose examples of said antagonists (modulators) of cADPR which are cADPR derivatives and include, 8-NH_2-cADPR, 8-Br-cADPR, 8-CH_3-cADPR. 8-OCH_3-cADPR and 7-Deaza-8-Br-cADPR (see page 11, 1st col., paragraph [0099]). **APPLICANTS:** This statement is not relevant to Applicants' claimed invention. Applicants disclose the use of AGONISTS of cADPR, not ANTAGONISTS as recited above. **EXAMINER:** The difference between applicant's claimed method and the method disclosed by Lund et al. is that Lund et al. do not exemplify the use of cADPR derivative to treat inflammation in a subject. However, Lund et al. teach that antagonists (modulators) of cADPR	[0099] In yet another embodiment of the invention, compounds that directly alter (i.e., activate or inactivate) the activity of cADPR, i.e., induced calcium release and cell migration, can be tested in assays. Such agonists or antagonists would be expected to modulate the influx of Ca2+ into the cell resulting in changes in the cell's migratory activity or ability to contract. Antagonists would have reduced Ca2+ responses, reduced contractility and/or reduced migration in the presence of a chemoattractant. Examples of antagonists include, but are not limited to 8-NH.sub.2-cADPR, 8-Br-cADPR, 8-CH.sub.3-cADPR, 8-OCH.sub.3-cADPR and 7-Deaza-8-Br-cADPR. A compound fitting these specifications is described in further detail in the working example of the present specification (Example 6, FIG. 10). Agonists would have

such as a cADPR derivative can be used to treat inflammation in a subject (see page 4, 2nd col. Paragraph [0032] and see page 11, 1st col., paragraph [0099]). **APPLICANTS**: Applicants agree that the Examiner's statement above, that "Lund et al. teach that antagonists (modulators) of cADPR such as a cADPR derivative can be used to treat inflammation in a subject," is a correct characterization of the teachings of Lund et al. concerning the use of ANTAGONISTS of cADPR.. However, this statement of the Examiner's IS NOT a correct statement of the Applicants' invention. As recited in claim 1, above, Applicants' method is directed to the use of cADPR, "or a FUNCTIONAL analogue or derivative thereof" to reduce the degree of an inflammatory condition in a patient. A compound that performs the same function as a first compound is an AGONIST of that compound, not an ANTAGONIST. Furthermore, the compounds recited by Lund et al. at paragraph [0099], being ANTAGONISTS of cADPR function rather than functional derivatives, or AGONISTS, would NOT work in Applicants' claimed method. Thus, the Examiner has not made even a *prima facie* obviousness argument in rejecting Applicants' claims. Instead, Applicants submit that Lund et al. is a clear teaching away situation and that one of ordinary skill would never have been led to the Applicants' invention through any of the Lund et al. teachings.	increased Ca2+ responses, increased contractility and/or increased migration in the presence of chemoattractants. Examples of agonists include but are not limited to 2'-deoxy-cADPR, 3'-deoxy-cADPR and 2'-phospho-cADPR. Assays for direct measurement of cAPDR activity include the bioassays such as those described by Howard et al. (1995, Science 262:1056); Galione et al. (1993, Nature 365:456-459) and Lee and Aarhus (1991, Cell Regulation 2:203-209).

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